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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/762,602	03/21/01	KAROUZAKIS	P 1581/128WO

002101
BROMBERG & SUNSTEIN LLP
125 SUMMER STREET
BOSTON MA 02110-1618

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EXAMINER	
HUI, S	
ART UNIT	**PAPER NUMBER**
1617	6

DATE MAILED: 05/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/762,602	KAROUZAKIS ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In addition, claim 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for misoprostal and misoprostol acid, does not reasonably provide enablement for other misoprostol metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There is no adequate direction provided by the applicant as to how to select any other suitable misoprostol metabolites to be used in the invention to treat female sexual dysfunction. Furthermore, the instant specification does not provide any working examples to show how any other misoprostol metabolites compounds besides misoprostal and misoprostol acid, may be used successfully in the invention to treat female sexual dysfunction.

Moreover, it is known in the art that different compounds may have different potency and activity because of the structural and conformational differences in the compounds. Therefore a different misoprostol metabolites, other than misoprostol acid, may be reasonably expected to yield a different result. Due to this unpredictability, it would prevent the skilled artisan from selecting a compound which may be termed an

"misoprostol metabolites" to retain the desired function of the instant invention to treat an female sexual dysfuncytion without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16, 18, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "an agent" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The expression "adverse effects arising from an otherwise toxic amount of misoprostol or the metabolite of misoprostol" in claim 14 renders the claim indefinite. It is unclear what amount of misoprostol or the metabolites of misoprostol is encompassed by the claims.

Claim 16 recites the limitation "the beneficial effect" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The term "low" in claim 18 is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to what degree of viscosity is encompassed by the claim.

Claim 26 recites the limitation "a pharmaceutical composition" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Cytotec monogrph, August 1995 in Physicians' Desk Reference, 54th ed. 2000, page 2907-2909.

The Cytotec monograph teaches a pharmaceutical composition contains misoprostol and hydroxypropyl methylcellulose (page 2907, Description section).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nahoum (US Patent 5,773,457) and Buyuktimkin et al. (US Patent 6,046,244) in view of El-Rashidy (US Patent 5,256,652), Lowrey (US Patent 5,981,563) and Reilly (chapter 80 in Remington: The Science and Practice of Pharmacy, page 1397, 1509-1512).

Nahoum teaches that both misoprostol (a prostaglandin E_1 analog) and alprostadil (a prostaglandin E_1) are useful in treating female sexual dysfunction (See col. 9, lines 47-48; lines 53- col.10, line 1).

Buyuktimkin et al. teaches that a topical prostaglandin E_1 (PGE_1) composition is useful for treating any disease that is treated by prostaglandin E_1 (see col.1, line 27-28 and col. 8, line 6-8). Buyuktimkin et al. also teaches the amount of the active prostaglandin ingredient to be 0.1-0.5 %w/v (See col. 10, Table 1). Buyuktimkin et al. also teaches that the composition can be cream or gel (See col. 7, lines 42-43). Buyuktimkin et al. also teaches that the topical PEG_1 composition comprises a penetration enhancing agent (See claim 1).

The primary references do not expressly teach that the topical sexual dsyfunction treating composition employs misoprostol particularly. The primary references do not expressly teach the application of the topical prostaglandin composition in a method of treating female sexual dysfuntion to the vagina or clitoris. The primary references do not expressly teach the female sexual dsyfunction treating method comprising a-cyclodextrin, gelatin, and hydroxymethylcellulose. The primary references do not expressly teach the female sexual dsyfunction treating method comprising hydroxypropyl methylcellulose in the amount of 4% w/v.

El-Rashidy teaches a topical sexual dsyfunction treating composition that comprises a vasodilating agent, a-cyclodextrin, and hydroxypropyl methylcellulose (See col. 3, line 67-68; col. 6, line 2-4). El-Rashidy also teaches that the amount of hydroxypropyl methylcellulose is 2-3%w/v (See col.8, Table II).

Lowrey teaches that the sexual response in females involve vasodilation and engorgement of the genitalia with arterial blood in a manner analogous to the male erectile response (See col. 5, line 38-51).

Reilly teaches that gelatin is useful as an emulsifying agent (page 1397, col. 1; also page 1511 col.2, examples section).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to apply a topical female sexual dysfunction treating composition of misoprostol with or without another vasodilator onto the vagina or clitoris. It would have been obvious for one of ordinary skill in the art at the time the invention was made to incorporate a-cyclodextrin, gelatin, and hydroxymethylcellulose, with the amount of 4%, into the topical female sexual dysfunction treating composition in a method to treat female sexual dysfunction.

One of ordinary skill in the art would have been motivated to apply the sexual dsyfunction treating composition, employing misoprostol, with or without another vasodilator, cyclodextrin, gelatin, and hydroxymethylcellulose, in the amount of 4%, onto the vagina or clitoris in a method to treat female sexual dysfunction because these agents are known to be useful in the treatment of sexual dysfunctions, including in female. Furthermore, it is known in the art that female sexual response is associated with vasodilation and engorgement of the genitalia with arterial blood. Therefore applying a composition containing known vasodilating agents, including the instant compounds directly onto any area of the genital would have been reasonably expected to be effective in treating female sexual dysfunction. Furthermore, incorporating known

topical pharmaceutical composition excipients such as a-cyclodextrin, gelatin, and hydroxymethylcellulose that are known to be useful additives in forming topical compositions is considered within the skill of artisan.

Optimization of result effect parameters (amount of ingredients) is obvious as being within the skill of the artisan.

Claims 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cytotec® monogrph, August 1995 in Physicians' Desk Reference, 54th ed. 2000, page 2907-2909 in view of Nahoum (US Patent 5, 773,457).

The Cytotec® monograph teaches a pharmaceutical composition contains misoprostol and hydroxypropyl cellulose (page 2907, Description section).

The Cytotec® monograph does not expressly teach that the pharmaceutical composition contains a second vasodilating agent.

Nahoum teaches that both misoprostol and alprostadil are useful in treating female sexual dysfunction (See col. 9, lines 47-48; lines 53- col.10, line 1).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to incorporate misoprostol, hydroxypropyl methylcellulose and a second vasodilating agent into a pharmaceutical composition.

One of ordinary skill in the art would have been motivated to incorporate misoprostol, hydroxypropyl methylcellulose and a second vasodilating agent into a pharmaceutical composition because combining two agents which are known to be

useful to treat sexual dysfunction individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Monday to Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moęzie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
May 21, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600